IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Lawrence Solomon, et al.

Serial No.: 10/598,315 Group Art Unit: 1615

Filed: April 8, 2008 Examiner: Sasan, A.

For: **SCORED PHARMACEUTICAL TABLETS COMPRISING A PLURALITY OF SEGMENTS**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR 1.132

I, David P. Beach, Ph.D., the undersigned, am a citizen and resident of the United States, and hereby submit the following as, to the best of my knowledge and understanding, being a true and accurate statement:

WHEREAS, I received a B.S degree in Pharmacy from Union University – Albany College of Pharmacy, in 1973; and a Ph.D. degree in Industrial Pharmacy from the University of Maryland at Baltimore (1982); and

WHEREAS, I have authored three (3) journal publications and one (1) chapter in a reference text; and

WHEREAS, I was a pharmacist in private practice and for private hospitals from 1973-1982;

WHEREAS, following my private practice as a pharmacist, I entered the commercial pharmaceutical industry and held the positions of:

- Solids Development Senior Scientist/Group Leader at DuPont Pharmaceuticals in Wilmington, DE from 1982-1987;
- Director, Formulations Research and Development at Superpharm Corporation in Central Islip, NY from 1987-1988;
- Manager, Animal Health Formulations Research; Manager, Process Improvement Group; and Associate Director, Pharmaceutical Process Improvement at Schering-Plough Corporation, Kenilworth, NJ from 1988-1992;
- Director, Research and Development at Genpharm Inc., Etobicoke, Ontario, Canada from 1992-1993;
- Vice-President Technical Operations and President and Board Member at TorPharm, a Division of Apotex Inc., Toronto, Ontario, Canada from 1993-2004;
- Senior Consultant at VCG&A, Toronto Ontario Canada from 2005-2007; and
- President and COO at Synovics Pharmaceuticals Inc. in 2007; and

WHEREAS, from 2007 to the present, I have served as a private consultant to the pharmaceutical industry, including specialization in manufacturing and process development for solid pharmaceutical dosage forms, and currently serve in that capacity to ACCU-BREAK Pharmaceuticals, Inc., and its subsidiary, ACCU-BREAK Technologies, Inc., which is the assignee in the subject application; and

WHEREAS, I have read and reviewed the subject patent application, as filed and amended, as well as the instant Office Action and the reference(s) cited therein.

NOW THEREFORE, BEING established as an expert in the field of pharmaceutical manufacture, and an expert on the subject matter of the claimed invention and the subject matter described and claimed in the reference CH 648754 to Hess (hereafter, Hess) cited against the claims of the instant application, I make the following statements and render my opinion based on my knowledge of the inventions and in view of my experience and expertise:

THAT, the Hess reference describes tablets that are distinguishable from the tablets claimed in the subject application. These distinctions include:

1. The tablets of the invention are expressly claimed as having a score on the bottom (active) segment or layer only, and having the inactive layer as the top layer. By contrast, Hess does not describe a tablet without a score on the top layer and provides only that the bottom layer is an inactive composition.

Figures 1-3, and the accompanying descriptions in Hess, as well as the specification and Examples, describe tablets having a score on their top surface. However, providing a score on the top surface requires the top punch of the tableting device to be embossed. An embossed top punch means that a tamping step cannot be performed on the first layer without forming an undesired indentation or trough in that first layer. A scored top layer, as described by Hess, also results in incomplete separation of the active layer into unitary segments. Hess does not describe tablets having the top layer as inactive, and only describes a tablet wherein the bottom layer is inactive ("S2, also as placebo layer present").

The tablets of the invention are scored on the bottom surface only, and scored in the bottom active segment, using an embossed bottom punch. The unscored inactive layer in tablets of the invention is specified as the top layer. Scoring of the bottom active layer using an embossed bottom punch allows for a) tamping of the first layer, and b) more complete separation of the active layer into unitary segments (see Appendix, described in more detail below).

2. The tablets of the invention require a uniform or level surface for each layer which is achieved by tamping the first layer – a score on the top surface of the tablet, as described by Hess, precludes tamping of the first layer.

The manufacture of the tablets of the invention includes scoring of the bottom active layer. No scoring of the top, inactive layer is provided in the tablets of the subject invention. This process allows an un-embossed top punch to be used as a "tamp" prior to disposition of the second, inactive composition forming the top layer.

The process of manufacturing the tablets according to Hess is carried out without a tamping step applied to the first layer. This omission of a tamping step is necessitated by the fact that Hess describes tablets which are scored on the top surface requiring the top punch to be embossed to form the score. Therefore, a tamping step must be omitted because tamping of the first layer or segment prior to disposition of the second layer using an embossed top punch disadvantageously forms an undesired indentation or trough in the top surface of the first layer.

The resulting indentation or trough is filled in by the second layer, forming a "bulged" interface which causes the scored area to have a "thickness" greater than if the embossing were on the bottom die or punch. The thickness of the score area allows a greater surface area of the active composition to be exposed when broken through, which can alter the release profile of the active from that composition.

In addition, without tamping of the first layer prior to disposition of the second composition, the first layer does not form a uniform surface to interface with the second composition. More specifically, Hess describes a process of forming a bi-layer tablet wherein the granulation having a particle diameter of up to 1 mm is added through a first hopper. Therefore, the granulation which was entered does not form a defined layer in the tablet die of the tableting machine. Rather the granulation forms a fill having a shape which is determined by the flow properties of the granulation. Assuming that the granulation is entered into the tableting die in the central portion of the die, the granulation will flow from the central portion of the die to the peripheral portions of the die. However, the granulation will accumulate in the central portion so that a planar surface of the layer cannot be formed. In case an embossing is present that rises from the lower punch in the central portion of the tablet die, and in case a layer is formed above the highest point of said embossing, the first granulation will accumulate above the embossing.

Accordingly, the second granulation entering the die, on top of said first granulation, will be distributed according to the flow properties of the second granulation. Given that the first granulation has accumulated in the central portion of the tableting die, the second granulation will preferentially flow toward the peripheral portion of the die.

The differences in the resulting tablets using an upper punch to produce a score, versus using an embossed lower punch and enabling the upper punch to be used for tamping, is shown in the attached Appendix. The Appendix includes photographs of tablets produced by the different processes as a result of experiments carried out previously under my supervision. As shown, when the score formed by the upper punch there is an extrusion or "bulging" of the upper layer into the first layer of the bilayer tablet. The photographs provided in the Appendix further illustrate that scoring of the tablet using an embossed top punch precludes tamping because tamping with an embossed top punch forms inadequate separation of unitary segments. Hess fails to describe or recognize the need for tamping of the initial (bottom) layer.

The configuration of the tooling to produce the tablets as described in Hess, WOULD NOT result in a uniform tamped layer, as there is score debossing on BOTH faces of the tablet. Therefore, a uniform interface between the layers of the tablet CANNOT result, and the dose uniformity then claimed for the segments would be lost. The same issue results from the tablet described in Figure 3A with scoring on BOTH faces of the tablet.

The score must ONLY be placed on one side of the tablet, not both, as compression of the active layer to a placebo or another active layer results in extrusion of the first active layer INTO the placebo or second active layer if the first active layer is not "tamped" to a uniform surface with a non-scored upper punch.

3. A tablet as described in the Hess reference is inoperable and cannot provide the features or advantages provided by the tablets of the invention.

Hess clearly describes processes and features that produce or result in tablets that are inoperable. Specifically, Hess fails to provide a process or tablet that employs tamping of the first layer. Without tamping of the first granulate with the upper punch to provide a uniform and level surface, it is impossible to provide a functional tablet because compression of the active layer to a placebo or another active layer results in extrusion of the first active INTO the placebo or second active layer. In addition, the weight of the second layer will not be uniform as the volume into which it is filled will vary depending on the filling of the die by the first layer, thus producing erratic dosing of at least the second layer if not BOTH layers.

Moreover, the maintenance of release rate from the tablets claimed by HESS would also be detrimentally affected by the scoring patterns depicted in the figures of HESS. The extended release from the described tablet results from the SLOW diffusion of the active drug from the compressed matrix, and is mathematically modeled using Fick's Law of Diffusion. This model, for a given matrix, demonstrates the DIRECT proportion between diffusion surface area and release rate, e.g. the larger the surface area for diffusion, the FASTER the release rate. Given that only a maximum of 40-50% of the tablet contains the described score, breakage of the tablet along the score would result in the production of a NEW surface for diffusion from the matrix, and therefore an INCREASE in the rate of release from the broken tablet segments. When coupled with the already described dosing issues (see above) based on the disclosed tooling design, these two factors would combine to produce a unacceptable final product from both a dosing and release rate perspective.

The dissolution claimed in the patent description of Hess CLEARLY indicates that the tablet segments were FASTER at all time points. Both of the actives used in the Hess tablets have "marginal" solubility and therefore, whether the invention or simply the physical chemical properties of the active pharmaceuticals used as examples contributed to the dissolution performance cited, is a matter of conjecture. In addition, since NO content uniformity data is presented, an assessment concerning the adequacy of dosing of the two examples presented cannot be made.

Hess further describes and depicts a tablet that includes a "band" around its perimeter wherein the face of the band is flat. Therefore any type of tablet coating operation (as described in the patent for these tablets) following compression will result in these flat surfaces adhering to one another resulting in "twins" which would produce an unacceptable final product.

THERFORE, the Hess reference clearly does not describe tablets that are the same, and does not provide adequate description that would lead a person to arrive at, a tablet having the features or advantages of the subject tablets.

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David P Beach

David P. Beach, Ph.D.

Date: 08/23/2011

APPENDIX

UPPER PUNCH SCORE VS. LOWER PUNCH SCORE

Prototype experiments -- Accu-Break bi-layer tablet technology

FIG. 1: Bi-layer tablet scored with embossed upper (top) punch

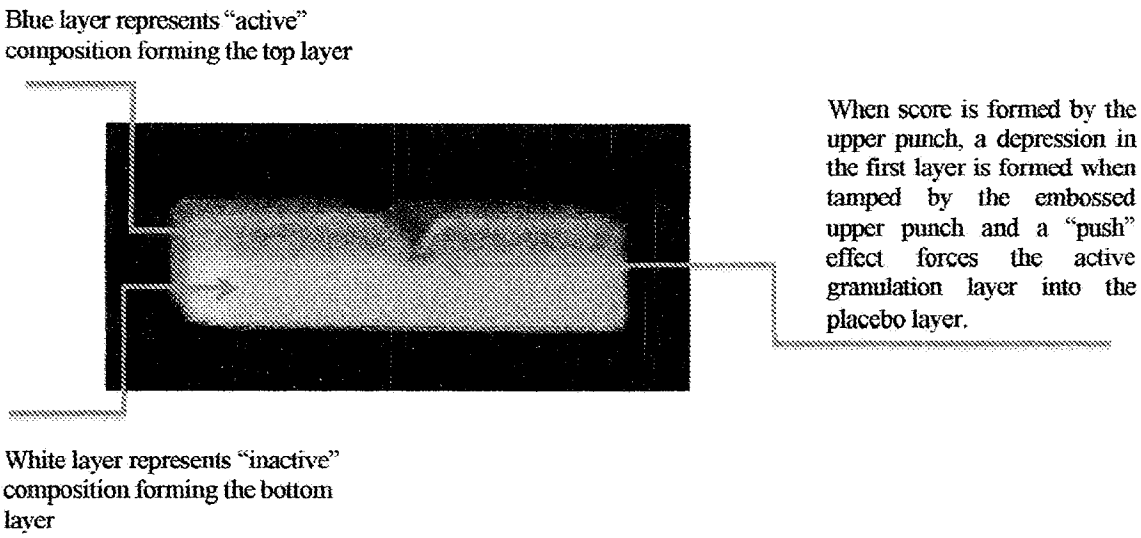

FIG. 2: Bi-layer tablet scored with embossed lower (bottom) punch